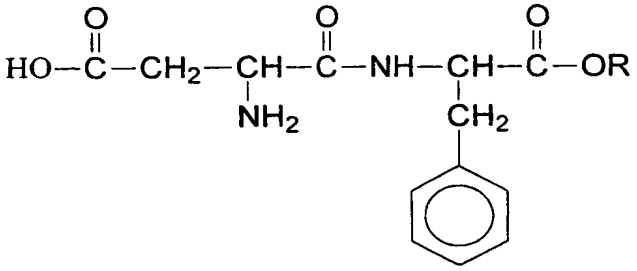
I CLAIM:

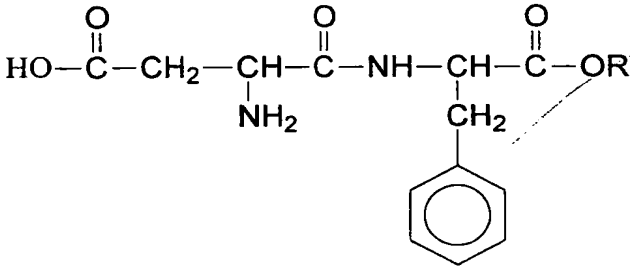
1. Use of the compound



where R is CH_3 or an alkyl to prepare a pharmaceutical composition useful for effecting a reduction in whole blood viscosity in a mammal.

2. The use of Claim 1, wherein said alkyl having 2 to 6 carbons.

3. A pharmaceutical preparation in dosage unit form adapted for administration to obtain a reduction in whole blood viscosity, comprising, per dosage unit, an effective, nontoxic amount of a compound comprising

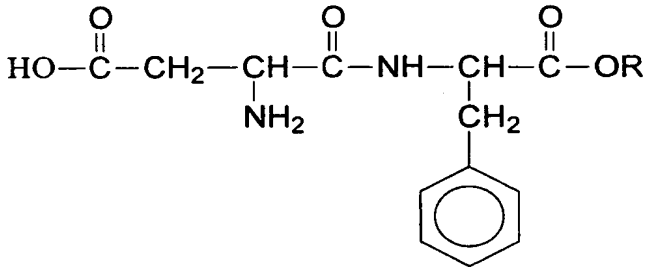


wherein R is CH_3 or an alkyl and a pharmaceutical carrier.

4. The pharmaceutical dosage form of Claim 3, wherein said alkyl having 2 to 6 carbons.

5. The pharmaceutical dosage form of Claim 3 or 4, wherein said dosage is from about 1 milligram to about 6 milligrams per kilogram body weight.

6. A method for treatment of high whole blood viscosity in a patient comprising administering in a treatment regimen to said patient an effective amount of a composition comprising



where R is CH_3 or an alkyl, wherein said treatment regimen is capable of reducing whole blood viscosity in said patient.

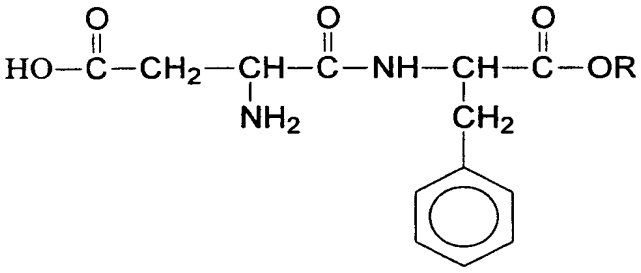
7. The method of Claim 6, wherein said alkyl having 2 to 6 carbons.

8. The method of Claim 6 or 7, wherein said effective amount is from about 1 milligram to about 6 milligrams per kilogram body weight.

9 A method for reducing whole blood viscosity in a patient blood sample, comprising the steps of:

a. collecting a blood sample from said patient; and

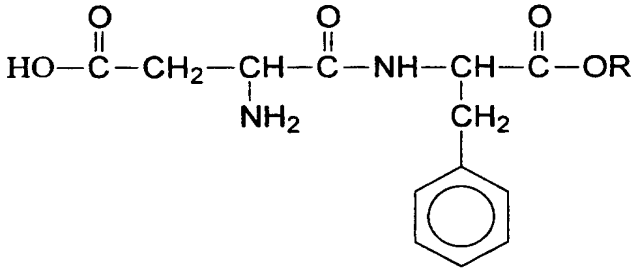
b. adding to said sample an effective amount of a composition comprising the compound



wherein R is CH_3 or an alkyl, wherein said effective amount causes a reduction in whole blood viscosity.

10. The method of Claim 9, wherein said alkyl having 2 to 6 carbons.

11. A method for monitoring the reduction of whole blood viscosity in a patient receiving treatment with a composition comprising



where R is CH_3 or an alkyl of 2 to 6 carbons, comprising:

a. at a first time point, collecting a blood sample from said patient to form a first patient sample;

b. measuring the viscosity of said first patient sample to obtain a first viscosity value;

c. at a second time point, collecting a blood sample from said patient to form a second patient sample;

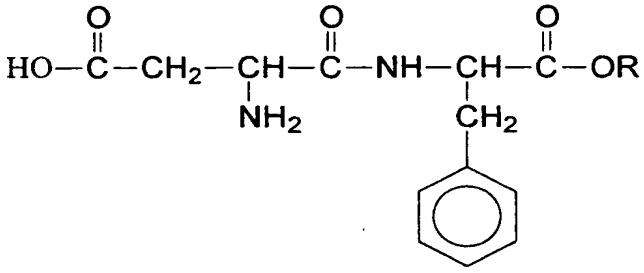
e. measuring the viscosity of said second patient sample to obtain a second viscosity value; and

f. comparing said second viscosity value to said first viscosity value,

wherein a reduction of viscosity is demonstrated by said second viscosity value being less than said first viscosity value.

12. The method of Claim 11, wherein said viscosity value is determined by drawing an aliquot of said patient sample into a pipette which is in a stationary vertical position and measuring the time required to expel a drop of said patient sample from said pipette using constant pressure to obtain a time interval as said viscosity value.

13. A screening method for determining if a patient's whole blood viscosity can be reduced by a treatment regimen with a composition comprising



where R is CH_3 or an alkyl of 2 to 6 carbons, comprising:

a. collecting a blood sample from said patient prior to administration of said composition to form an untreated patient sample;

b. measuring the viscosity of said untreated patient sample to obtain a baseline viscosity value;

c. administering to said patient said composition at an amount from about 1 milligram to about 6 milligrams per kilogram body weight;

d. after administrating said composition to said patient, collecting a blood sample from said patient to form a treated patient sample;

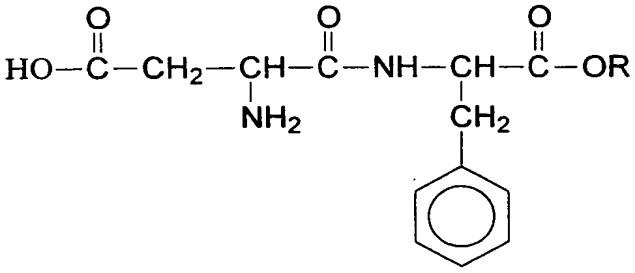
e. measuring the viscosity of said treated patient sample to obtain a post-treatment viscosity value; and

f. comparing said post-treatment viscosity value to said baseline viscosity value,

wherein said post-treatment viscosity value being less than said baseline time viscosity value demonstrating said composition is capable of reducing whole blood viscosity in said patient and wherein said post-treatment viscosity value being greater than or equal to said baseline viscosity value demonstrating said composition is not capable of reducing whole blood viscosity in said patient.

14. The method of Claim 13, wherein said viscosity value is determined by drawing an aliquot of said patient sample into a pipette which is in a stationary vertical position and measuring the time required to expel a drop of said patient sample from said pipette using constant pressure to obtain a time interval as said viscosity value.

15. A method for treating a patient having a disease characterized by abnormally viscous whole blood comprising administering in a treatment regimen to said patient an effective amount of a composition comprising



where R is CH_3 or an alkyl, wherein said treatment regimen is capable of reducing whole blood viscosity in said patient.

16. The method of Claim 15, wherein said alkyl having 2 to 6 carbons.

17. The method of Claim 15 or 16, wherein said effective amount is from about 1 milligram to about 6 milligrams per kilogram body weight.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 April 2001 (05.04.2001)

PCT

(10) International Publication Number
WO 01/22983 A3

(51) International Patent Classification[7]: A61K 38/05, G01N 33/49, A61P 7/00

(21) International Application Number: PCT/US00/25874

(22) International Filing Date:
21 September 2000 (21.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/156,119 25 September 1999 (25.09.1999) US

(71) Applicant *(for all designated States except US)*: OKLAHOMA MEDICAL RESEARCH FOUNDATION [US/US]; 825 NE 13th Street, Oklahoma City, OK 73104 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: MANION, Carl, V. [US/US]; 6313 Overcourt Manor, Oklahoma City, OK 73132 (US).

(74) Agents: HANSEN, Eugenia, S. et al.; Sidley & Austin, Suite 3400, 717 North Harwood, Dallas, TX 75201 (US).

(81) Designated States *(national)*: AU, CA, MX, US.

(84) Designated States *(regional)*: European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published:
— *with international search report*

(88) Date of publication of the international search report:
16 August 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/22983 A3

(54) Title: VISCOSITY MODULATING SUBSTANCE AND USE THEREOF

(57) Abstract: It has now been found that N-L-alpha-aspartyl-L-phenylalanine 1-methyl ester (APM) lowers whole blood viscosity in patients, including those suffering from sickle cell disease and plasma cell dyscrasias. Upon in vivo APM treatment, patients experienced a significant lowering of whole blood viscosity. In vitro addition of APM to patients samples having elevated whole blood viscosity resulted in reduced viscosity over time. These in vitro and in vivo results identify APM as a therapeutic agent for molecular diseases which lead to elevated whole blood viscosity. A method by which APM treatment can be monitored is also disclosed.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/25874

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/05 G01N33/49 A61P7/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, MEDLINE, CANCERLIT, CHEM ABS Data, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 00692 A (OKLAHOMA MED RES FOUND ;EDMUNDSON ALLEN B (US); MANION CARL V (US)) 9 January 1997 (1997-01-09) cited in the application page 39, line 17 -page 44, line 15 --- -/--	1-17

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 March 2001	23/03/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Stein, A

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1979 POKROVSKII A V ET AL: "HEMO RHEOLOGICAL DISORDERS IN PATIENTS WITH ATHERO SCLEROTIC LESION OF THE ABDOMINAL AORTA AND THEIR CORRECTION USING ASPIRIN" Database accession no. PREV198069069702 XP002162682 abstract & KARDIOLOGIYA, vol. 19, no. 2, 1979, pages 54-61, ISSN: 0022-9040	
A	MANION C V ET AL: "SICKLE CELL DISEASE AND ASPARTAME." CLINICAL PHARMACOLOGY & THERAPEUTICS,US,MOSBY-YEAR BOOK, ST LOUIS, MO, vol. 65, no. 2, February 1999 (1999-02), page 194 XP000891777 ISSN: 0009-9236 the whole document	1-17
P,X	WO 00 18418 A (EDMUNDSON ALLEN B ;MANION CARL V (US); OKLAHOMA MED RES FOUND (US)) 6 April 2000 (2000-04-06) cited in the application page 12, line 14 - line 18 page 19, line 1 -page 21, line 10 claims 1-29	1-17
P,X	MANION C V ET AL: "SICKLE CELL VISCOSITY ALTERATION WITH ASPARTAME" CLINICAL PHARMACOLOGY & THERAPEUTICS,US,MOSBY-YEAR BOOK, ST LOUIS, MO, vol. 67, no. 2, February 2000 (2000-02), page 102 XP000891560 ISSN: 0009-9236 the whole document	1-17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/25874

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9700692 A	09-01-1997	US 5654334 A	05-08-1997
		AU 722460 B	03-08-2000
		AU 6287896 A	22-01-1997
		CA 2225462 A	09-01-1997
		EP 0833651 A	08-04-1998
		JP 2000502318 T	29-02-2000
		US 5998473 A	07-12-1999
WO 0018418 A	06-04-2000	AU 6400899 A	17-04-2000

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
11146/11002		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/25874	21/09/2000	25/09/1999

International Patent Classification (IPC) or national classification and IPC
A61K38/00

Applicant
OKLAHOMA MEDICAL RESEARCH FOUNDATION et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18/04/2001	07.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Deck, A Telephone No. +49 89 2399 8432

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25874

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-14	as originally filed

Claims, No.:

1-14	as received on	12/10/2001	with letter of	12/10/2001

Drawings, sheets:

1/3-3/3	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 3-5.12-14.

because:

☒ the said international application, or the said claims Nos. 3-5, 12-14 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-14

	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	see separate sheet

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

S ction III:

Claims 3-5, 12-14 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Section V:

1. The following documents have been considered:

   D1: WO 97 00692 A (OKLAHOMA MED RES FOUND ;EDMUNDSON ALLEN B (US); MANION CARL V (US)) 9 January 1997 (1997-01-09) cited in the application

   D2: MANION C V ET AL: 'SICKLE CELL DISEASE AND ASPARTAME.' CLINICAL PHARMACOLOGY & THERAPEUTICS,US,MOSBY-YEAR BOOK, ST LOUIS, MO, vol. 65, no. 2, February 1999 (1999-02), page 194 XP000891777 ISSN: 0009-9236

2. Claims 1-14 are new and inventive as none of the prior art describes nor suggests the anti-viscosity activity of aspartame or its derivatives.

3. For the assessment of the present claims 3-5, 12-14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VIII:

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO-A-0018418	06.04.2000	25.09.1999	25.09.1998

The priority of this document is validly claimed. Its content could therefore be relevant in the national phases.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 17 July 2001 (17.07.01)	
International application No. PCT/US00/25874	**Applicant's or agent's file reference** 11146/11002
International filing date (day/month/year) 21 September 2000 (21.09.00)	**Priority date** (day/month/year) 25 September 1999 (25.09.99)
Applicant MANION, Carl, V.	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

18 April 2001 (18.04.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer H. Zhou
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

10/088713

Copy for the Elected Office (EO/US)

PCT/US00/25874

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

HANSEN, Eugenia, S.
Sidley & Austin Brown & Wood
Suite 3400
717 North Harwood
Dallas, TX 75201
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)
23 April 2002 (23.04.02)

Applicant's or agent's file reference
11146/11002

IMPORTANT NOTIFICATION

International application No.
PCT/US00/25874

International filing date (day/month/year)
21 September 2000 (21.09.00)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address
HANSEN, Eugenia, S.
Sidley & Austin
Suite 3400
717 North Harwood
Dallas, TX 75201
United States of America

State of Nationality

State of Residence

Telephone No.
214-981-3315

Facsimile No.
214-981-3400

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
HANSEN, Eugenia, S.
Sidley & Austin Brown & Wood
Suite 3400
717 North Harwood
Dallas, TX 75201
United States of America

State of Nationality

State of Residence

Telephone No.
214-981-3315

Facsimile No.
214-981-3400

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
Anne BEUCHAT

Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994)

004810157

1887

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
11146/11002		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 25874	21/09/2000	25/09/1999
Applicant		
OKLAHOMA MEDICAL RESEARCH FOUNDATION et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
T/US 00/25874

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/05 G01N33/49 A61P7/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, MEDLINE, CANCERLIT, CHEM ABS Data, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 00692 A (OKLAHOMA MED RES FOUND ;EDMUNDSON ALLEN B (US); MANION CARL V (US)) 9 January 1997 (1997-01-09) cited in the application page 39, line 17 -page 44, line 15 --- -/--	1-17

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
13 March 2001	23/03/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Stein, A

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1979 POKROVSKII A V ET AL: "HEMO RHEOLOGICAL DISORDERS IN PATIENTS WITH ATHERO SCLEROTIC LESION OF THE ABDOMINAL AORTA AND THEIR CORRECTION USING ASPIRIN" Database accession no. PREV198069069702 XP002162682 abstract & KARDIOLOGIYA, vol. 19, no. 2, 1979, pages 54-61, ISSN: 0022-9040 ---	
A	MANION C V ET AL: "SICKLE CELL DISEASE AND ASPARTAME." CLINICAL PHARMACOLOGY & THERAPEUTICS,US,MOSBY-YEAR BOOK, ST LOUIS, MO, vol. 65, no. 2, February 1999 (1999-02), page 194 XP000891777 ISSN: 0009-9236 the whole document ---	1-17
P,X	WO 00 18418 A (EDMUNDSON ALLEN B ;MANION CARL V (US); OKLAHOMA MED RES FOUND (US)) 6 April 2000 (2000-04-06) cited in the application page 12, line 14 - line 18 page 19, line 1 -page 21, line 10 claims 1-29 ---	1-17
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
/US 00/25874

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		AU 722460 B	03-08-2000
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